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(54) Title: CONTROLLING IMMUNE RESPONSE TO SPECIFIC ANTIGENS

(57) Abstract

One major problem with adenovirus gene therapy has been the T-cell mediated immune response elicited by inoculation of adenovirus, which leads to rapid clearance of the virus and loss of transgene expression. In the instant invention, the immune response to a virus is prevented by pre-treatment with adenovirus, adenoassociated virus or herpes virus infected antigen-presenting cell (APC) expressing Fas ligand with induced T-cell tolerance. Administration of AdCMVLacZ after tolerance resulted in prolonged expression of LacZ in tolerized animals compared to control treated animals. In control, but not tolerized animals, there was proliferation of $CD3^+$ T-cell in the spleen in response to AdCMVLacZ treatment. Tolerance induction is also indicated by decreased production of interferon-γ and IL-2 by peripheral T-cells isolated from treated animals after stimulation with the adenovirus infected APCs. T-cell tolerance is specific for the virus as the T-cell responses to an irrelative virus, mouse cytomegalovirus (MCMV) remained unimpaired. The instant invention utilizes virus specific T-cell tolerance, which is induced by APCs that co-express Fas ligand and virus antigens. The instant invention involves novel vectors and methods to induce tolerance to a viral vector gene therapy and prolong expression of a transgene in a viral host.